OIPE
SEP 25 1998
PATENT & TRADEMARK OFFICE
JC57

#13
Dey
10/8/98
1/3

PATENT
RPP135fUS

RECEIVED
SEP 29 1998
GROUP 1800

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Molly F. Kulesz-Martin Art Unit: 1642

Serial No: 08/811,361

Filed: March 4, 1997

Examiner: Bansal, G.

For: p53as PROTEIN AND ANTIBODY THEREFOR

I certify that this **APPEAL BRIEF** is being deposited on **September 21,1998** with the U.S. Postal Service as first class mail addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

Michael L. Dunn, Registration No. 25,330

APPEAL BRIEF
(37 CFR 1.192)

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants respectfully appeal the decision of the Examiner finally rejecting Claim 11 as set forth in the Office Action dated March 18, 1998. A Notice of Appeal was timely filed by the Applicants on July 20, 1998.

Real Parties in Interest

09/28/1998 00000018 08811361
01 FC:220 155.00 OP

The real parties in interest are Health Research Inc., Assignee of the entire interest. Assignment recorded on September 23, 1993 on Reel 6696, Frames 993-995 for parent application serial number 08/100,496, from which this is a divisional application.

Related Appeals and Interferences

There are no related appeals or interferences.

Status of Claims

The application originally contained 1 claim (Claim 11) which remains in the Application. Claim 11, the only claim on appeal, is set forth in the Appendix.

Status of Amendments

Claim 11 has been amended. No amendments have been offered which have not been entered.

Summary of the Invention

The invention is a **purified** peptide which peptide (in unpurified form) is present in p53as protein of a mammal and is identical to the unique carboxy terminal region of p53as which distinguishes p53as protein from p53 protein. The **purified** peptide contains a unique epitope which is not present in p53.

Issues Presented for Review

Whether Claim 11 is patentable under 35 USC 112, apparently for indefiniteness or undue breadth (although the exact basis is not stated).

Whether Claim 11 is patentable under 35 USC 102(b) over Arai et al, Molecular and Cellular Biology, September 1986, vol. 6, pp 3232-3239.

Grouping of Claims

There is only one claim.

Argument

Claim 11 is patentable under 35 U.S.C. 112.

In the final rejection, the Examiner said: "With respect to the argument that a sequence identity is not required and that the metes and bounds will be understood by one of skill in the art, it is stated again that any peptide can be made from the choice of 20 amino acids and strung together in a huge number of sequences from two amino acids long to twenty amino acids long."

The Examiner is missing an important point. In particular, the peptide **claimed** is unique, i.e. being "identical to the unique carboxy terminal region of p53as which distinguishes p53as protein from p53 protein" **and** "containing a unique epitope which is not present in p53".

p53 for any animal can be readily sequenced and this has in fact been done for many mammals. This is now an essentially "cookbook" operation once the p53 is isolated. Similarly p53as, according to the present specification and parent application, can also be readily sequenced and this also has been done. One skilled in the art may therefore now determine the unique carboxy terminal region of p53as as compared with p53 without even leaving a desk. It can also be readily determined whether the carboxy terminal region contains a unique sequence by comparison with already known p53 sequences. Once it is known that there is a unique sequence in a carboxy terminal end of a p53, it is a simple matter to determine whether it will raise an antibody with which p53 does not react. The presence of a unique epitope is thus readily determined and established. There is no problem for one skilled in the art to practice the invention and in such a case a specific sequence need not be provided or deposited.

The objection to the term "p53as protein" is unwarranted. "p53as protein" has been clearly defined in the specification, i.e., it is essentially identical to p53 up to the final 50 carboxy terminal amino acids. The final 50 amino acids of p53as lack the negative regulatory domain of p53 and the final 50 amino acids of p53as contain a unique epitope not found in p53. There is no requirement in the law that a generic claim to a peptide be accompanied by a sequence I.D. number. All that is necessary is that the metes and bounds of the claim be understood and they would be understood here by one skilled in the art.

It is clearly established law that a patent attorney may be his or her own lexicographer. "p53as protein" is clearly defined in the specification and claims. An unduly restrictive sequence I.D. number is not required.

Assuming that the sequences are identical in the p53as and the p53as peptide, probabilities are very high that the unique nature of the sequence as an epitope will be retained in the peptide as it has been shown that p53 retains activity by simple truncation.

There is no ambiguity.

Claim 11 is not anticipated or suggested by Arai et al.

The Examiner has rejected Claim 11 as being anticipated by Arai et al.

This is not an appropriate rejection for at least two reasons. In the first place, Arai et al. does not disclose or suggest a purified peptide which contains an epitope which distinguishes from p53.

In the absence of the teachings of the present application, there is no reason to extract any particular peptide from the Arai et al. non-functional sequence, terminal or otherwise, even though the technology is available to extract a given peptide. For peptides of lengths 2-20 (lengths previously assumed by the Examiner) the number of possible peptides is 7670. There is no suggestion of why a sequence, similar to the presently claimed peptide, should be isolated and purified from the Arai et al. 7670 possible peptides. The use of the present disclosure for the purpose of isolating and purifying one of the 7670 possible peptides of Arai et al. is impermissible hindsight. The fact that the sequence in Arai may also be terminal (unpurified and not even in a protein) is irrelevant. Arai et al. teaches no significance for a terminal sequence in p53as and certainly not isolated. The 7670 possible peptides of Arai et al. is in stark contrast with the minimal numbers of peptides for a given p53as as presently claimed and as previously discussed.

Arai et al. clearly does not anticipate or suggest the presently pending claim.

Secondly, the alternatively spliced p53 of Arai et al. is not a p53as as presently claimed. p53as is a perpetually active form of p53 since it lacks the negative regulatory domain of p53 and p53as contains a unique epitope which is not present in p53.

By contrast, the sequence of Arai et al. is not suggested as being active at all nor does Arai et al. suggest that the Arai et al. sequence is present in normal cellular environments. Arai et al. obtained his structure from chemically transformed cells not from normal cells. The amino acid sequence predicted (not prepared or isolated in whole or in part) by Arai, referred to by the Examiner, is not the purified p53as terminal

sequence claimed but is unpurified and embedded in a predicted, not even existing, protein. The sequence in Arai et al. is not purified.

The rejection under 35 USC 102 is therefore improper on its face. Arai et al. does not disclose any separate peptides and certainly not the one presently claimed.

Furthermore, the entire Arai et al. sequence is not p53as. The final nucleic acids of the encoding sequence of Arai et al. simply do not match the encoding sequence of p53as of either naturally occurring p53 or naturally occurring p53as.

Please note that the clone of Arai et al. is distinct from p53as in structure and function. In structure, it has a mutation of the p53 gene coding region whereby a cyst residue at amino acid 132 is replaced by a phe residue. See Arai et al., 1986, page 3236 for entire coding sequence of p53-M-8 with the change noted.

In function, the M-8 clone lacks the properties of P53as. p53as has the properties of p53 including:

1. binding efficiently and specifically to the p53 consensus sequence in DNA and forming tetramers (see Kulesz-Martin et al., Mol. Cell. Bio., pp. 1698-1708, March 1994, and Wu et al., EMBO, Vol. 13, pp. 4823-4830, 1994; and

2. transcriptional activation suppression of growth. (Wu et al., PNAS, pp. 8982-8987, August 1997).

M-8 has properties of <u>mutant</u> p53 including:

1. transforming cells rather than suppressing transformation (Eliyahu et al., Oncogene 3:313-321, 1988); and

2. forming monomers and dimers, not tetramers (Hainaut and Milner, EMBO 11:3513-3520, 1992).

There is no reason, teaching or suggestion in any of the cited art for taking a specific region of mutant p53, translating it and making a specific peptide from it. The specific peptide in accordance with the present invention, has utility with respect to p53as activity but has no utility at all with respect to the cited M-8 mutant which has no p53 type activity at all.

Conclusion

In view of the foregoing, it is clear that the pending claim is patentable under 35 U.S.C. 112 and over the cited prior art under both 35 U.S.C. 102 and 35 U.S.C. 103. Reversal of the Examiner and allowance of all claims are therefore respectfully requested.

Respectfully submitted,

Dated: September 21, 1998

Michael L. Dunn
Attorney for Applicant(s)
Reg. No. 25,330
P.O.Box 96
Newfane, New York 14108
Telephone: (716) 433-1661

MLD/csc

Appendix

Reprinted below is the claim on appeal:

11. A purified peptide designated p53as peptide which peptide is present in p53as protein of a mammal and is identical to the unique carboxyl terminal region of p53as which distinguishes p53as protein from p53 protein, said peptide containing a unique epitope which is not present in p53.